

### **Remarks/Arguments**

Applicant wishes to thank the Examiner for the courtesy of an interview on July 22, 2003, attended in person by the Examiner and Applicant/Inventor Dr. Babak Nemat and joined by Jean Ellis, J.D., an associate attorney for Applicant, via telephone. The Examiner's comments in clarifying the rejections set forth in the present Office Action were most helpful and greatly assisted Applicant in preparation of the present response.

The claim amendments are submitted to put the claims in better form for allowance and/or in better form for consideration on appeal, and were made after considering points raised by the Examiner during the interview. The 132 Declaration is submitted to support these claim amendments. Reconsideration and entry of the amendment is respectfully requested.

### **In the Specification**

By the present amendment, Applicant has amended the title of the application to more particularly describe the presently claimed invention, which is directed to methods to enhance optical transparency of biological tissue.

### **In the Claims**

Applicant acknowledges the renumbering of previously submitted new claims 17-31 as claims 70-84.

Claims 70-84 were pending prior to this response. By the present communication, claims 70, 71, 77, and 83 have been amended to define Applicant's invention with greater particularity and put them in better condition for allowance. Claim 85 has been added to define a specific embodiment of the invention. The amendments add no new matter, being fully supported by the Specification and original claims:

Amendment to claims to specify that the method “transiently” enhances transparency through a “target” tissue finds support throughout the Specification, including page 1, paragraph 1; page 5, first paragraph; Examples B and C.

Amendment to claims to specify that “light transmission through the tissue is improved after local delivery of the clarifying agent as compared to before such delivery” is supported by the Specification at least at page 2, first paragraph; page 9, first paragraph; Figures 2-5; Examples A and B.

Amendment to claims to specify that the clarifying agent is locally delivered is supported throughout the Specification by reference to delivery to target tissue, and at page 5, first paragraph, where “local delivery” is inferred by avoidance of collateral, or non-local, tissue.

Amendment to the claims to specify “an effective amount” of clarifying agent is supported throughout the Specification, including Examples A and B, and page 8, paragraph 1, where the concept of “effective amount” is understood from the passage describing the amount of glycerol applied to be effective at clearing edematous corneas; and page 2, second paragraph, where the phrase “effective amount” is understood from the passage describing the need for a sufficient volume of clarifying agent to reach the target tissue.

Amendment to the claims to specify “interstitial space” is supported throughout the Specification, including at page 15, first paragraph.

Amendment to claim 70 to recite (b) contacting the surface permeability barrier with a means for applying a driving force ..; and (c) applying the driving force directly to the surface permeability barrier.. is supported throughout the Specification, including at pages 16-19, where numerous means for applying a driving force are disclosed, wherein the means physically contacts the surface permeability barrier and applies the driving force directly to the surface permeability barrier, e.g., means for electroporation or

iontophoresis (e.g., patches or needles), concentration gradient, mechanical device for removing stratum corneum).

New claim 85 is supported by the original claims and the Specification.

Accordingly, claims 70-85 are currently pending in the application.

#### **The Rejection under 35 U.S.C. §102(e)**

Claims 70, 71, 74, 75 and 76 were rejected under 35 U.S.C. §102(e) as being anticipated by Chan et al. (US 6,275,726; "Chan"). The Examiner stated that Chan discloses a method of delivering a glycerol clarifying agent past a surface permeability layer of skin to covered biological tissue to enhance optical transparency, and that the agent is used in treatment of patients. The Examiner also stated that the Chan delivery includes jet injection, which applies physical force to the agent to force it through the barrier layer.

As amended, claim 70 recites that the means that applies the driving force physically contacts the surface permeability barrier and, further, that the driving force is applied directly to the surface permeability barrier. Thus, the means for applying the driving force is in physical contact with the permeability barrier and the driving force is applied directly to the permeability barrier. As discussed during the interview, these claim elements are not met by using jet injection as a means to deliver a driving force. The Applicant/inventor has provided a Declaration under 37 C.F.R. 1.132, attached hereto as Appendix I and incorporated herein, stating his understanding that, in contrast to means employed in the presently claimed invention, a device for applying a jet injection force is positioned apart from the surface that is to receive the jet injection force. This occurs either as a function of the apparatus design, whereby a built-in spacer separates the driving mechanism from the target tissue surface, or the operational design, whereby the jet injector device does not contact the target tissue. The Declaration references two internet addresses where these distinctions are animated and drawn, respectively.

It is for these reasons that claim 70 is distinct from the disclosure of Chan with respect to the possible use of jet injection. Because Chan does not disclose each and every element of claim 70, and claims 71, 74, 75, and 76 dependent from claim 70, Chan does not anticipate the invention claimed in claims 70, 71, 74-76. Applicant respectfully requests reconsideration and withdrawal of the rejection.

**The Rejection under 35 U.S.C. §103(a)**

Claims 72, 83 and 84 are rejected under 35 U.S.C. §103(a), as being unpatentable over Chan in view of Edwards (US 5,833,647; "Edwards"). The Examiner alleges Chan discloses the claimed invention except for the delivery of an agent past barrier tissue by sonophoresis, electroporation, temperature gradient, or iontophoresis, and that use of these methods is taught by Edwards to deliver drugs past barrier tissue for treatment of a patient. The Examiner asserts it would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Edwards in the method of Chan in order to effectively deliver an agent past the barrier tissue.

Claims 73 and 77-82 are rejected under 35 U.S.C. §103(a), as being unpatentable over Chan in view of Weaver (US 5,019,034; "Weaver"). The Examiner alleges Chan discloses the claimed invention except for the delivery of an agent past barrier tissue by concentration gradient, optical pressure, or solvent, and that use of these methods is taught by Weaver to deliver molecules and agents past barrier tissue. The Examiner asserts it would have been obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Weaver in the method of Chan in order to effectively deliver fluids past the barrier tissue.

Claims 83 and 84 are rejected under 35 U.S.C. §103(a), as being unpatentable over Chan in view of Henry (J. Pharm. Sci. 87(8):992-925; "Henry"). The Examiner alleges Chan discloses the claimed invention except for the delivery of an agent using microneedles to increase skin permeability, and that Henry teaches using microneedles to deliver agents past the stratum corneum. The Examiner asserts it would have been

obvious to one of ordinary skill in the art at the time of the invention to use the teachings of Henry in the method of Chan in order to effectively deliver molecules to tissue covered by the stratum corneum barrier.

Applicant respectfully traverses these rejections. It is well established that rejection of claims under 35 U.S.C. §103(a) on the basis of a combination of references must be supported by some suggestion, motivation, or teaching that would have led a person of ordinary skill in the relevant art to select the references and make the combination to reach the rejected claims. Such motivation may be found in the references themselves, from knowledge of those skilled in this art, or from the nature of the problem to be solved. In the present case, the Examiner alleges that the requisite motivation to combine Chan with each of Edwards, Weaver, and Henry is found in the problem to be solved, stating:

“...all the references are concerned with methods to bypass the barrier layer of skin to deliver agents to covered tissue. The references show that it is well known in the art to use different methods to achieve this delivery. One of ordinary skill in the art would know by these references of the availability and desirability of the different methods, each having its own benefits.” (page 4, second paragraph of Office Action)

and

“... all the references are concerned with the same problem of delivering agents across the skin barrier and the various methods recited in the claims are shown to be well known established methods of delivering agents to covered tissue.” (page 4, third paragraph of Office Action)

Applicant respectfully disagrees with the Examiner's conclusion and, in the Declaration attached hereto as Appendix I, stating his reasons for believing that the presently claimed invention is patentable under 35 U.S.C. §103. In brief, the Declaration states that:

(a) Chan addresses a different problem than Edwards, Weaver, and Henry. Chan is focused on delivering replacement fluid to a target tissue (e.g., skin) covered by a barrier (e.g., stratum corneum) for the purpose of temporarily increasing the light transmission through the skin. In contrast, Edwards, Weaver, and Henry focus on delivery of therapeutic agents for a systemic, long term medicinal effect. Due to the disparity in problems to be solved, it is farfetched to allege that one of skill in the art of optical transparency enhancement would look to the systemic drug delivery art for guidance on delivery of an agent for local, temporary enhancement of optical transparency.

(b) Lack of motivation to combine references. As set forth in the Declaration (Appendix I), Applicant outlines that he has special expertise in the areas of optics and lasers, ophthalmology, electrically-assisted drug delivery and other applications, and that such special expertise is not found in one of ordinary skill in the art. It is this special expertise that led Applicant to the present invention, and it argues against one of ordinary skill having sufficient knowledge of the benefits of combining aspects of one art with the other in the manner suggested by the Examiner. Thus, at the time Applicant made his invention, one of ordinary skill in the art would not have had sufficient knowledge in these disparate arts to be motivated to combine art related to systemic drug delivery with art directed to delivery of an agent for local, temporary enhancement of optical transparency,

(c) No reasonable expectation of success if references were combined. As discussed by Applicant in the Declaration (Appendix I), the goal of the secondary references is to deliver drug to the blood stream for a long term therapeutic effect. Therefore, it is not surprising that none of Edwards, Weaver, or Henry discloses how to deliver a drug (let alone an optical enhancing agent) such that an effective amount will be retained locally at the target site to have a transient effect. Because of the insufficiency of the disclosures, one of ordinary skill would not have reasonably expected that the systemic drug delivery methods of Edwards, Weaver and Henry could be used to locally deliver an optical enhancing agent disclosed by Chan. Thus, even if one did combine the references in the manner suggested by the Examiner, there could be no reasonable

expectation that the systemic drug delivery methods of Edwards, Weaver and Henry would successfully achieve local delivery of an optical enhancing agent disclosed by Chan.

Accordingly, neither the references nor knowledge of one skilled in the art would have provided motivation for one of ordinary skill in this art to combine the Chan reference with any of Edwards, Weaver and Henry, at the time the present invention was made. Based on the foregoing, Applicant respectfully requests reconsideration and removal of the rejection under 35 U.S.C. §103(a).

#### **Request for an Interview**

Should there be any remaining issues after entry of the amendment and consideration of the remarks herein, Applicant respectfully request either an in-person interview or a telephonic interview with the Examiner.

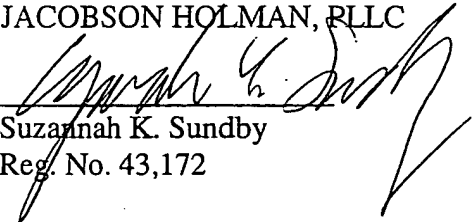
#### **Conclusion**

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. It is believed that a full and complete response has been made to the outstanding Office Action and, as such, the present application is in condition for allowance.

It is not believed that extensions of time are required, beyond those that may otherwise be provided for in accompanying documents. However, in the event that additional extensions of time are necessary to prevent abandonment of this application, then such extensions of time are hereby petitioned under 37 C.F.R. §1.136(a), and any

fees required therefor are hereby authorized to be charged to our Deposit Account No.  
06-1358, referencing Attorney Docket No. P66960US1.

Respectfully submitted,  
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